Epidermal Remodeling in Psoriasis (II): A Quantitative Analysis of the Epidermal Architecture

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Hyperproliferative psoriatic epidermis was quantitatively analyzed using a geometric model of viable epidermis. Our model was based on hexagonally arranged cylindrical papillae, which allowed the determination of the total volume of the viable epidermis and the total area of the interface with the proliferative compartment based on several parameters, such as papillary height, papillary width, and distance between neighboring papillae. The analysis assumed that the total number of viable epidermal cells paralleled the proliferative compartment in a steady state of cell flow, so a quantitative relation could be made between both volume and interface of the viable epidermis. Multiple parameters of the psoriatic epidermal architecture were measured, and variations within psoriasis were predicted by the model. The results predicted were remarkably close to the observed values. The geometric model also indicated that psoriatic epidermis could be subdivided into two distinct types, with and without a granular layer; the latter having a shorter turnover time. This is consistent with the notion that the typical psoriatic epidermis (without the granular layer) represents the expanding hyperproliferative phase, whereas the psoriatic epidermis with a granular layer represents stationary or resolving states. The model of hexagonally arranged cylindrical papillae suggested that the architecture of the psoriatic epidermis is constructed by a simple mechanism, whereby the psoriatic angulated rete-papilla pattern was produced by a two-dimensional increase in the proliferative compartment and a three-dimensional increase in the total volume of the viable epidermis. *Key words: geometric model/granular layer/turnover time. J Invest Dermatol 109:806–810, 1997*

Hyperproliferative psoriatic epidermis is characterized by the downward elongation of the rete ridges to a relatively uniform position in the dermis. The marked extension of the psoriatic dermo–epidermal interface results in a greatly increased number of germinative basal cells compared with normal epidermis. An expansion of cell number can also be detected in the differentiating compartment, and these alterations form the characteristic "psoriasiform" angulated rete-papilla pattern (Lever and Schaumburg-Lever, 1990). We have previously reported that the epidermis of the psoriatic architecture can be described using a novel concept of epidermal remodeling, related to epidermal turnover time, as defined by total cell number divided by the rate of new cell production in a steady state (Iizuka *et al*, 1996). Thus, hyperproliferation results from an expansion of cell number of both differentiating and proliferative compartments that enlarge to maintain the "minimal turnover time" (Iizuka, 1995; Iizuka *et al*, 1996). The minimal turnover time is required because each compartment has a minimal time to accomplish the processes that define each compartment. Whereas an increase of cells can simply overlie the differentiating compartment, the greater adhesiveness of germinative cells to the basement membrane, which has been detected in the normal epidermal keratinocytes (Watt, 1984; Jones and Watt, 1993; Bata-Csorgo *et al*, 1993), results in an extension of the dermo–epidermal interface in the proliferative compartment, forming the "psoriasiform" angulated architecture.

There is, however, a marked variation in the architecture of psoriatic epidermis. Although a single specimen may be relatively uniform, there is variation in the rete-papillae pattern, particularly in the depth of dermal papillae, between individuals. The process of keratinization, which is closely related to the turnover time (Iizuka *et al*, 1996), also varies, and for example, contrary to the accepted definition, it has long been known that the granular cell layer is occasionally observed even in the typical psoriatic lesion (Cox and Watson, 1972). To validate the epidermal remodeling concept, it is necessary to explain this variability.

In the present study, quantitative analysis was performed using the epidermal remodeling concept, assuming that the total number of viable epidermal cells was parallel to the proliferative compartment in a steady state of cell flow. A model of hexagonally arranged cylindrical papillae was constructed, and multiple parameters by actual measurement of the psoriatic epidermis were established, which correlated extremely well with the theoretical values predicted by the model.

MATERIALS AND METHODS

Materials The epidermal tissue was obtained from typical cases of classical plaque psoriasis, retrieved from archival histologic samples from the Department of Dermatology, Asahikawa Medical College, which had been routinely taken over the period 1978–96. The specimens had been fixed with 10% formalin, processed routinely, and stained with hematoxylin and eosin. Only samples with papilla height (H) more than 100 μm were analyzed (total 50 cases).

Measurements The horny layer was not included in the measurement. The parameters measured were as follows: H, papilla height; W, papilla width; A, rete ridge width; B, thickness of suprapapillary epidermis; C, height of basal

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Abbreviations: G-minus psoriasis, psoriatic epidermis without granular layer; G-plus psoriasis, psoriatic epidermis with granular layer.

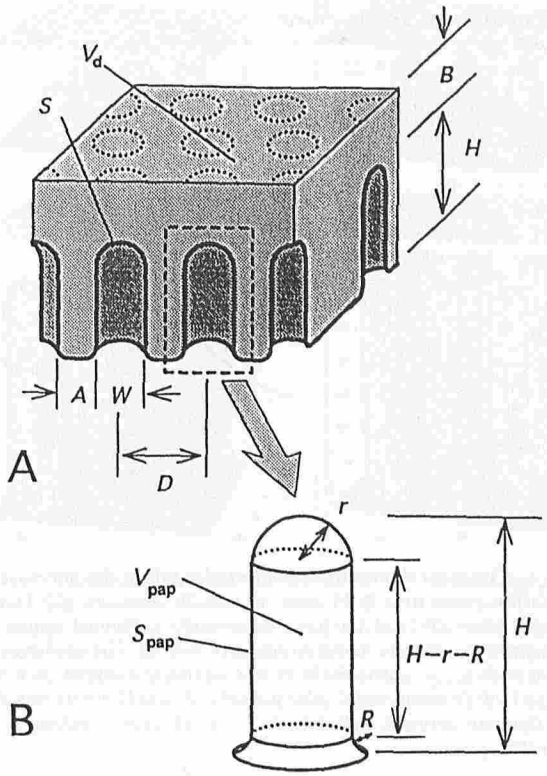

Figure 1. Hexagonally arranged cylindrical papilla model. (*A*) Dermal papillae are hexagonally arranged in the model. (*B*) Each papilla consists of a cylinder with a hemispherical cap (radius r). The cylinder also has a rim (radius R) that does not overlap with those of neighboring papillae. H, papilla height; W, papilla width (= 2r); A, rete ridge width; D, distance between neighboring papillae (= W + A); B, thickness of suprapapillary epidermis; V_d, total volume of the differentiating compartment in a column (1 × 1 mm); S, total interface of the differentiating compartment facing the proliferative compartment in the column; V_{pap}, volume of a papilla; S_{pap}, interface of a papilla facing to the differentiating compartment.

cells. In vertical sections of optical micrography, W corresponds to the width of the widest papillae, whereas A corresponds to the width of the narrowest rete ridges. These measured values were confirmed by horizontal sections of optical micrography. H and B correspond to the lengths of the longest papillae and the narrowest suprapapillary portions, respectively. To compensate for variation within a single specimen, three typical areas were selected from each specimen and the average values were used for analysis. Periappendageal skin (near hair follicles and sweat ducts) was excluded from measurements. The distance between neighboring papillae, D, was calculated to be W + A. Although the granular layer was not expected to be present in typical psoriatic epidermis, it was occasionally observed in the real samples, so the epidermal architectures with or without the granular layer were separately recorded.

A model of hexagonally arranged cylindrical papillae For the purposes of this model, dermal papillae are assumed to be cylindrical in shape and regularly arranged in a hexagonal manner (Iizuka *et al*, 1996) (**Fig 1*A***). Although the proliferative compartment is known to comprise heterogeneous populations of stem cells and transient amplifying cells with differing cell cycle time (Lavker and Sun, 1983; Potten and Morris, 1988), they were assumed to be uniform with an arbitrary cell cycle time in the present analysis. Additionally, although the size of keratinocytes is substantially larger in the upper epidermis, the average volume of single cells of the proliferative and differentiating compartments were arbitrarily defined as v_p and v_d, respectively.

A column perpendicular to the skin surface and its horizontal cross-section is considered a square (1 × 1 mm), and the volumes of the differentiating epidermal compartment, V_d, and proliferative epidermal compartment, V_p, in the column have been estimated. The proliferative epidermal compartment attaches to the dermo–epidermal interface. Dermal papillae are cylinders protruding from dermis into epidermis, which are assumed to be the same shape and arranged hexagonally. The hexagonal arrangement holds the maximal number of the same-sized papillae (with accompanying epidermis) per unit square.

A single papilla is a cylinder of diameter W μm and height H μm with a hemispherical cap of radius r μm (W = 2r, **Fig 1*B***). Papillae also have small rims with a curl of radius R μm, with no overlap with neighboring papillae. The distance between neighboring papillae is D μm and the thickness of suprapapillary epidermis is B μm. Then,

$$V_d(H, W, D, B) = (H - 2/\sqrt{3}\cdot V_{pap}/D^2 + B)\cdot 10^6 \quad (1)$$

where $V_{pap} = 2\pi r^3/3 + \pi r^2(H - r - R) + \pi R(r + R)^2 + 2\pi R^3/3 - \pi^2R^2(r + R)/2$. The area of the epidermal–dermal interface is

$$S(H, W, D) = \{2/\sqrt{3}\cdot S_{pap}/D^2 + 1 - 2/\sqrt{3}\cdot\pi(r + R)^2/D^2\}\cdot 10^6$$

where $S_{pap} = 2\pi r^2 + 2\pi r(H - r - R) + \pi^2R(r + R) - 2\pi R^2$. The proliferative epidermal compartment, V_p, is calculated as

$$V_p(H, W, D, C) = C\cdot S(H, W, D) \quad (2)$$

because the proliferative compartment is thin with a thickness of C μm.

Assumption of the steady state of cell flow The hypothesis being tested is that psoriatic epidermal architecture is constructed by a self-organizing mechanism, which can be visualized by comparing the theoretical values from the model with the real measured parameters. The analysis is based on an assumption that the total number of viable epidermal cells parallels that of the proliferative compartment in the steady state of cell flow. As described below, this is directly related to the concept of epidermal turnover time.

The cell numbers in differentiating and proliferative epidermal compartments are V_d/v_d and V_p/v_p, respectively, where v_d and v_p are the average volumes of single cells. In our analysis, V_d can be approximated to be the total viable epidermal volume, because C is relatively small in the psoriatic samples with papilla height more than 100 μm.

The psoriatic epidermis can be histologically divided into two types, one without a granular layer and the other with a granular layer. The typical psoriatic epidermis has a markedly increased cell production rate resulting in a decreased turnover time (Iizuka *et al*, 1996), and can be recognized histologically as a hyperplastic epidermis without a granular layer. On the other hand, stationary and resolving psoriatic lesions show a decreased cell production rate, with more time for keratinization processes, and thus show a granular layer (Iizuka *et al*, 1996).

When the psoriatic epidermis belongs to one subtype, according to the assumption that the total number of viable epidermal cells parallels that of the proliferative compartment in the steady state of cell flow,

$$(V_d/v_d)/(V_p/v_p) = (V'_d/v'_d)/(V'_p/v'_p)$$

When using the formula (2),

$$(V_d/v_d)/(S\cdot C/v_p) = (V'_d/v'_d)/(S'\cdot C'/v'_p)$$

where $V'_d = V_d(H', W', D', B')$, $V'_p = V_p(H', W', D', C')$, and $S' = S(H', W', D')$. The properties, v_p, v_d, and C are considered to be the same within the subtype, i.e., $v_p = v'_p$, $v_d = v'_d$, and $C = C'$. Then,

$$V_d/S = V'_d/S' \quad (3)$$

and so $V'_d/V_d = S'/S$, i.e.,

$$V_d(H', W', D', B')/V_d(H, W, D, B) = S(H', W', D')/S(H, W, D) \quad (4)$$

The formula (4) shows that the four parameters H, W, D, and B are not independent with each other. For example, W can be calculated theoretically using the formula (4) and the other seven parametric values H, H′, W′, D, D′, B, and B′ given in **Table I**. D can be similarly calculated using seven other parameters (H, H′, W, W′, D′, B, and B′) in **Table I**.

Analysis of epidermal turnover time The rate of cells entering from the proliferative compartment into the differentiating compartment is $p\cdot V_p/v_p$, where p is the probability rate of cells in the proliferative compartment to enter the differentiating compartment per day. Obviously, in the steady state, p is equal to the cell production rate in the proliferative compartment. The turnover time of the differentiating epidermal cells in the steady state is

$$T_d = (V_d/v_d)/(p\cdot V_p/v_p) = (V_d\cdot v_p)/(S\cdot C\cdot p\cdot v_d) \quad (5)$$

Within the same subtype of psoriasis T'_d would be described as follows,

$$T'_d = (V'_d/v'_d)/(p'\cdot V'_p/v'_p) = (V'_d\cdot v'_p)/(S'\cdot C'\cdot p'\cdot v'_d)$$

As $v_p = v'_p$, $v_d = v'_d$, $C = C'$, and $p = p'$ within the same subtype of psoriasis in the steady state,

$$T'_d/T_d = (V'_d/S')\cdot(S/V_d)$$

When using (3), then

Table I. Measured parameters of psoriatic epidermal architecture[a]

Parameters	G-minus psoriasis, N = 28	G-plus psoriasis, N = 22
W	0.05643H + 53.79 (r = 0.3747)	63.68 ± 19.67 (–0.00706H + 65.13, r = 0.0296)[b]
D	0.09588H + 86.66 (r = 0.4793)	109.5 ± 20.67 (0.03254H + 102.8, r = 0.1300)[b]
B	46.39 ± 15.28	56.46 ± 15.92
C	11.00 ± 2.248	11.26 ± 2.107

[a] Regression lines by the least square method or means ± SD are described (μm). N, sample number; r, correlation coefficient of the regression.
[b] Regression line that was close to average line. Calculation in the report was performed using average line. For papilla distance, see **Fig 2*D*** (——).

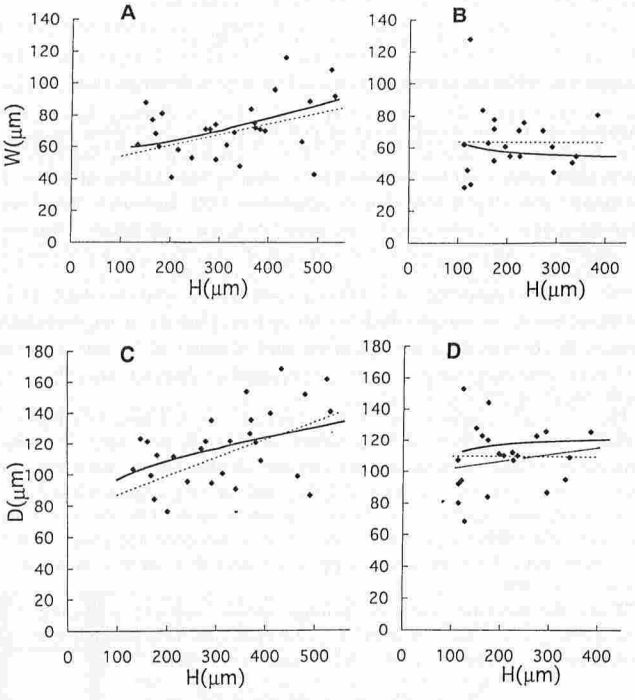

Figure 2. Measured W and D values plotted against H. The measured parametric values, W and D, from the psoriatic lesions without granular layer (*A, C*) and with granular layer (*B, D*) were plotted against H, and the regression lines by the least square method (*A, C*), and the average lines (*B, D*) are shown by *broken lines*. The average line in (*B*) was almost the same as the regression line. The average line in (*D*) should be compared with the regression line presented by the *thin solid line* (see **Table I**). The theoretical lines predicted by the model were also drawn (*thick solid line*).

$$T'_d = T_d$$

Thus the assumption that the total number of viable epidermal cells parallels that of the proliferative compartment has introduced the turnover time to be the same within each subtype of psoriasis. We can obtain the turnover time by the formula (5).

Calculation by a computer Software Mathematica (ver. 2.2, Wolfram Research, Champaign, IL) was used to resolve the equations and to obtain explicit parameter values from ones implicit in the equations.

RESULTS

Psoriatic epidermis without granular layer (G-minus psoriasis) and with granular layer (G-plus psoriasis) In the present analysis only samples with a papilla height (H) greater than 100 μm were used. Samples with a papilla height less than 100 μm had shown an irregular rete-papilla pattern, which made the measurement of morphologic parameters difficult, so the model of hexagonally arranged cylindrical papillae could not be convincingly applied. Although typical psoriatic epidermis should not have a granular layer, many real psoriatic samples did show a granular layer (Ishida-Yamamoto *et al*, 1996). In the pilot study, these two populations were distinct, and so they were separately analyzed.

The parameters H, W, D, B, and C, in the epidermis of G-minus (without granular layer) and G-plus (with granular layer) psoriasis were measured. The relationship of W *versus* H and D *versus* H were plotted as shown in **Fig 2**. W and D in the G-minus psoriasis showed some correlation with H (**Fig 2*A,C***), but other parameters including W and D in the G-plus psoriasis (**Fig 2*B,D***) showed no distinctive correlation with H. Variation in D was noted at lower values of H in G-plus psoriasis (**Fig 2*D***). The numerical results of the analysis are shown in **Table I**.

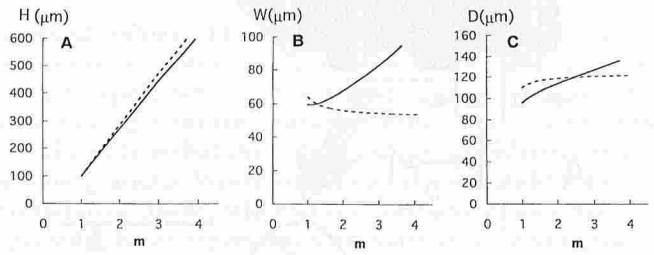

Figure 3. Theoretical parameters plotted against the increase in cell proliferation ratio m. (*A*) H *versus* m; (*B*) W *versus* m; (*C*) D *versus* m. Parametric values (W and D) were theoretically computed against H, and plotted against the increase in cell proliferative ratio m. The epidermis without (——) or with (- - - -) granular layer was separately analyzed. H is increased with m in both G-minus and G-plus psoriasis. W and D are increased with m in the G-minus psoriasis, whereas they are relatively constant in the G-plus psoriasis.

The analytical calculations leading to the theoretical parametric values were close to the actual values When H was considered to be variable, V_d(H, W, D, B) could be considered as a function of H, i.e., V(H) = V_d(H, W(H), D(H), B). When we put V_0 = V(100), m = V/V_0 = $(V/v_d)/(V_0/v_d)$ is defined as the cell proliferation ratio, where $(V/v_d)/(V_0/v_d)$ is a ratio of cell numbers of the differentiating compartment when the papilla height is H *versus* when the papilla height is 100 μm. The equation

$$V_d(H, W(H), D(H), B)/V_d(100, W(100), D(100), B) = m$$

was resolved with respect to H. Then, we obtained H = H(m), which is shown as H *versus* m in Fig 3*A*. In similar ways, W *versus* m and D *versus* m were obtained from

$$V_d(H(m), W, D(H(m)), B)/V_d(100, W(100), D(100), B) = m$$

and from

$$V_d(H(m), W(H(m)), D, B)/V_d(100, W(100), D(100), B) = m$$

respectively (**Fig 3*B,C***).

The calculated values for the papilla height H increased with the cell proliferation ratio m in both G-minus and G-plus psoriasis (**Fig 3*A***). On the other hand, the calculated parameters W and D in relation to m markedly differed between the G-minus and G-plus psoriasis. Whereas W and D of G-minus psoriasis increased with m (**Fig 3*B,C***, *solid lines*), W and D of G-plus psoriasis were relatively constant irrespective of m (**Fig 3*B,C***, *broken lines*). This resulted in a significant difference especially in W between the G-minus and G-plus psoriasis at higher values of m.

Figure 3(*B,C*) show the W and D values in G-plus and G-minus psoriasis theoretically estimated from the model of hexagonally arranged cylindrical papillae. These values could be compared with the actual values, and the theoretical curves of W and D against papilla height

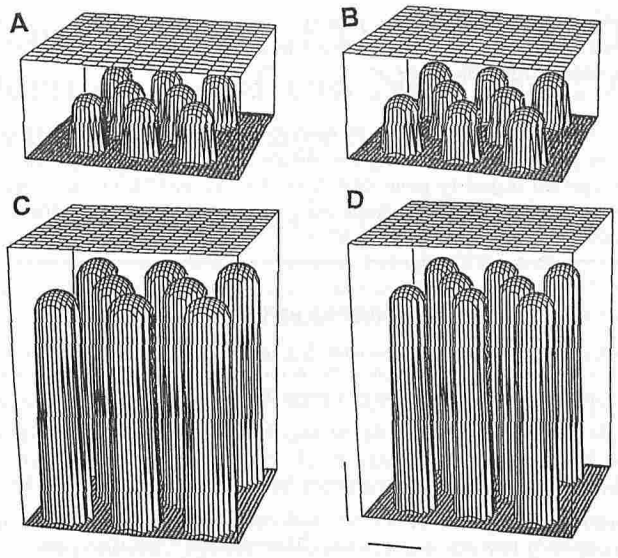

Figure 4. Three-dimensional presentation of simulated psoriatic epidermis. (*A*) G-minus psoriatic epidermis. H, W, D, B are 100, 59, 96, 46 μm, respectively; (*B*) G-plus psoriatic epidermis. H, W, D, B are 100, 64, 110, 56 μm, respectively; (*C*) G-minus psoriatic epidermis. H, W, D, B are 400, 76, 125, 46 μm, respectively; (*D*) G-plus psoriatic epidermis. H, W, D, B are 400, 64, 110, 56 μm, respectively. Note that W and D are considerably larger in G-minus psoriasis at H = 400 μm. Vertical and horizontal bars show about 100 μm, respectively.

H were plotted in **Fig 2** (*solid line*). The curves were close to the regression lines by the least square method or the average lines (*broken line*). Notably, although W and D were increased with H in G-minus psoriasis (**Fig 2*A*,*C***), they were relatively constant in G-plus psoriasis (**Fig 2*B*,*D***) in both theoretical and measured analyzes. Further, the theoretical W was apparently larger than the real W in G-minus psoriasis, and vice versa in G-plus psoriasis (**Fig 2*A*,*B***).

The epidermal turnover time is longer in G-plus psoriasis than in G-minus psoriasis Previous analysis has indicated that the architecture of the psoriatic epidermis is affected by epidermal turnover time (Iizuka, 1995; Iizuka *et al*, 1996). The ratio of the turnover times of G-minus and G-plus psoriatic epidermis was estimated using the model as follows. Analytical calculations gave the values of formula (4) in the two types of psoriasis, and the following relation was the result:

$$(V^+_d/(S^+\cdot C^+))/(V^-_d/(S^-\cdot C^-)) = 1.28 \qquad (6)$$

where + and − refer to parameters of G-plus and G-minus psoriasis, respectively. The formula is written using (5) as

$$((T^+_d\cdot p^+\cdot v^+_d)/v^+_p)/((T^-_d\cdot p^-\cdot v^-_d)/v^-_p) = 1.28$$

Assuming that $v^+_p = v^-_p$ and $v^+_d = v^-_d$,

$$T^+_d/T^-_d\cdot(p^+/p^-) = 1.28$$

Thus the following relation was obtained:

$$T^+_d/T^-_d = 1.28\cdot(p^-/p^+) \qquad (7)$$

Formula (7) indicates that the turnover time of the differentiating compartment depends on epidermal cell proliferative state in the steady state of cell flow. G-plus epidermis results in the prolonged turnover time, independent of the papillary height H. The proliferative rate of G-minus psoriatic epidermis p^- is usually considered to be larger than the proliferative rate of G-plus epidermis p^+; however, even if the G-minus and G-plus psoriatic epidermis shows the same proliferative rate, i.e., $p^+ = p^-$, there remains a difference in the turnover time; the G-plus psoriasis showed a longer turnover time of the differentiating epidermal compartment by a factor of 1.28.

G-minus and G-plus psoriasis have distinct three-dimensional views The representative figures of G-minus and G-plus psoriasis predicted by the model are shown in Fig 4. A notable difference in the three-dimensional view between G-minus and G-plus psoriasis was found at H = 400 μm. W is considerably larger in G-minus psoriasis than in G-plus psoriasis (**Fig 4*C*,*D***). Thickness of suprapapillary epidermis, B, is larger in G-plus psoriasis. These alterations made S, the area of the epidermal–dermal interface, larger in G-minus psoriasis.

DISCUSSION

These results indicate that the architecture of the psoriatic epidermis is explained by a simple mechanism that can be quantitatively adapted to real samples; there are hidden relations among the morphologic parameters that are obscured in a conventional view. By a simple assumption that the number of total viable epidermal cells is parallel to that of proliferative compartment in the steady state of cell flow, and by applying the model of hexagonally arranged cylindrical papillae, a "psoriasiform" architecture could be reconstructed that was mostly consistent with the real psoriasis. The psoriatic angulated rete-papilla pattern was shown to be produced by a two-dimensional increase in the proliferative compartment and a three-dimensional increase in the total volume of the viable epidermis.

It must be noted that there is a notion that psoriatic keratinocytes overexpress cell survival gene product and that they resist induction of apoptosis relative to normal keratinocytes (Wrone-Smith *et al*, 1995), findings that obviously influence the psoriatic architecture. Our approach, however, is to obtain evidence for a self-organizing mechanism in psoriasis, that can be visualized by comparing the model with the real measured parameters. In other words, parameter(s) of cell survival and death (apoptosis), if present, would be intrinsically incorporated in the architectural parameters, i.e., determined by the psoriatic architecture itself.

Our results indicate that whether the psoriatic epidermis has a granular layer gives distinct differences (**Figs 2, 3, 4, Table I**), with turnover time of G-plus epidermis being longer than the G-minus epidermis. If the G-plus epidermis has the same probability rate p to enter the differentiating compartment as the G-minus epidermis, it has a longer turnover time (of the differentiating epidermal compartment) by a factor of 1.28. This is consistent with the notion that an expanding hyperproliferative psoriatic lesion does not show granular layer, whereas the resolving lesion does (Krueger *et al*, 1995). As resolving lesions have a longer turnover time due to decreased cell production rate, the granular layer that had not been available and indistinct in the hyperproliferative condition would be visualized (Iizuka *et al*, 1996). It has been reported that the turnover time of normal and psoriatic epidermis is around 45–47 d (Bergstresser and Taylor, 1977; Iizuka, 1994) and 5.25 d (Weinstein *et al*, 1985), respectively. Normal epidermis has not been dealt with, but only psoriatic epidermis with papillary height of more than 100 μm. The relation in samples with H less than 100 μm was beyond the power of the present analysis.

These results indicate that H, W, and D of the G-minus typical psoriasis increased with the expansion of the cell proliferation ratio m (**Fig 3**). In the G-plus psoriasis W and D were relatively constant, whereas H increased with m.

In summary, these findings can be elaborated by the concept of epidermal remodeling (Iizuka *et al*, 1996). H is proportional to m in both G-minus and G-plus psoriasis, explaining that the higher proliferative ratio m makes H larger in both subtypes (**Fig 3*A***). As the expanding (G-minus) psoriasis must reconstruct the architecture including an upward expansion of papillary dermis, a significant force would be required. That force is provided by an increase in cell production ratio m in G-minus psoriasis. During the process the newly formed enormous number of cells must go up to the skin surface mainly through the pathway recognized as rete ridges. Consequently, the width, A, of rete ridges would be enlarged in the expanding hyperproliferative (G-minus) psoriasis. All these processes are caused by an enormous number of cells from a markedly enlarged proliferative compartment accompanying an increased papilla width, W. (Note that W is the parameter that is related to the size of proliferative compartment.) Consequently, D, the sum of A and W, would be increased, resulting in the enlargement of the psoriatic lesional area. This is depicted by parallel increases in W and D in relation to m in G-minus

psoriasis (**Fig 3**). In addition, the enlargement of D will form an expanding force on the surface of the psoriatic lesion, and might explain the relatively flat epidermal surface of psoriasis.

On the other hand, stationary or resolving psoriasis with a granular layer has a relatively decreased cell production rate gaining more turnover time (Iizuka *et al*, 1996). Consequently, W, the parameter of the size of the proliferative compartment, decreases (**Fig 3**). As the expanding force for W does not exist in the less hyperproliferative condition, W was naturally decreased. Thus W remains relatively constant and low in relation to m, whereas the papilla height H is directly proportional to m in the G-plus psoriasis (**Fig 3**). This is also consistent with a significant difference in W at higher values of H between G-plus and G-minus psoriatic epidermis (**Figs 2*A*,*B*, 4**). The decrease in W makes the area, S, of epidermal–dermal interface that corresponds to the proliferative compartment, smaller in G-plus psoriasis. This would also result in the decrease in D, especially at higher values of H (**Figs 2*D*, 3**). It is interesting to note that G-plus psoriasis tends to show an uneven surface at the uppermost viable epidermis, contrary to the flat surface of G-minus psoriasis (Cox and Watson, 1972). This comes from the diminution of D, and consequently the diminution of the lesional area, in the G-plus psoriasis at higher values of H.

It is also interesting to note that the measured W was apparently smaller than the theoretical W in G-minus psoriasis, and vice versa in G-plus psoriasis (**Fig 2*A*,*B***). Because W is the parameter of the size of the proliferative compartment, this means that the expanding G-minus psoriasis should enlarge the proliferative compartment by additional suprabasal mitoses; otherwise it cannot supply enough cell production determined by the model. This has long been documented in the literature; the typical psoriatic epidermis shows a significant amount of suprabasal mitoses (see, for example, Weinstein *et al*, 1985; van Neste *et al*, 1988). On the other hand, in a regressing G-plus psoriasis, the measured W is more than that required by the model, and the model predicts that the G-plus psoriasis would be able to maintain the architecture without significant suprabasal mitoses.

In conclusion, our model of hexagonally arranged cylindrical papillae is useful to understand the real psoriatic architecture, when quantitative analysis is based on the simple assumption that the increase in the total epidermal cell number is parallel to the increase in the size of the proliferative compartment in the steady state of cell flow. The same assumption would be applicable to other epidermal architectures, such as verrucous papillomas, as well as invasive carcinomatous tumors. The epidermal architecture appears to be constructed by a simple mechanism, consistent with the concept that a local self-organizing process results in a highly ordered epidermal architecture (Honda *et al*, 1996), that includes psoriasiform one.

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